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Hannsjorg Sinn

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EXAMINER

RUSSEL, JEFFREY E

ART UNIT

PAPER NUMBER

1654

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

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1. The proposed amendment to claim 1 reciting a methotrexate:albumin molar ratio of 1:1000 to 2:1 raises new issues requiring further consideration and/or search. Such a molar ratio range has not previously been claimed, and at a minimum would likely require a new ground of rejection under 35 U.S.C. 103(a) on the basis that determining the molar ratio of components in a conjugate is prima facie obvious. The examiner has noted Applicant's discussion of the possibility of submitting a declaration under 37 CFR 1.132 to establish criticality of the proposed claimed molar ratio range. The examiner will enter and consider any declaration under 37 CFR 1.132 filed before the filing of an Appeal Brief. See MPEP 716.02(d)(II) concerning the demonstration of criticality of a claimed range. Especially important for such a showing of criticality will be tests done just below, at, and just above the upper endpoint of the proposed molar range, i.e. methotrexate:albumin = 2:1.

The proposed molar range, and especially that part of the range embracing methotrexate:albumin molar ratios of less than 1:1, also raises issues under 35 U.S.C. 112, second paragraph. Because there are not, e.g., 1000 potential conjugation sites in a methotrexate molecule, it is not possible to conjugate 1000 molecules of albumin to 1 molecule of methotrexate (in order to achieve a methotrexate:albumin molar ratio of 1:1000). The proposed molar ratio range may imply the presence of unconjugated albumin in the conjugate, which appears to be self-contradictory.

2. The other proposed amendments to the claims contained in the amendment after final rejection would have been entered, and would have overcome the objections and rejections set forth in sections 2-6 and 9 of the final Office action. Proposed amended claims 15, 20, and 22 would continue to be rejected under 35 U.S.C. 103(a) for the same reasons set forth in section 10

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of the final Office action. It is prima facie obvious to determine reactant ratios in a chemical reaction.

3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (571) 272-0969. The examiner can normally be reached on Monday-Thursday from 8:00 A.M. to 5:30 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Cecilia Tsang can be reached at (571) 272-0562. The fax number for formal communications to be entered into the record is (571) 273-8300; for informal communications such as proposed amendments, the fax number (571) 273-0969 can be used. The telephone number for the Technology Center 1600 receptionist is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Jeffrey E. Russel/  
Primary Examiner, Art Unit 1654

JRussel  
March 11, 2009